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Patent 0-06-225/16799/US/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor:	Haj-Yehia, Abdullah I.
Serial no.:	10/532,390
Filed:	October 24, 2003
Title:	STEROID COMPOUNDS COMPRISING SUPEROXIDE DISMUTASE MIMIC GROUPS AND NITRIC OXIDE DONOR GROUPS, AND THEIR USE IN THE PREPARATION OF MEDICAMENTS
Examiner:	Sara Clark
Art Unit:	4121
Confirmation	8417

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir/Madam:

SUPPLEMENTAL RESPONSE TO NON-FINAL OFFICE ACTION

This supplemental response is being submitted to ensure claim 42 is amended correctly. We added brackets to certain terms in claim 42 to ensure that "–H or" was deleted; so it reads as follows: (Currently amended) A compound according to claim 31 wherein R^2 and R^5 are [~~is H or~~] —ONO_2.

This response is in reply to the office action mailed on April 28, 2009.

Claims Amendments

1. The amendments shown on the attached marked-up pages address the Examiner's rejections.

The objected term "solvates thereof" has been deleted.

Main claim 31 has been amended to the compounds having structure IVc (supported on pages 51-52 of the original specification) in which R^2 and R^5 are NO donors; R^3 is H, OH, or CH_3; R^1 is H or ONO_2; and R^9 and R^{10} are alkyl groups.

Claims 40-42 and 44 have been amended by (a) amending the substituents, or (b) deleting the subject matter incorporated into the main claim.

Claims 32-39, 43, and 45 have been canceled.

No new matter has been added.

Specification Amendment

2. Page 93 has been amended, in accordance with the Examiner's request to correct the chemical name of Compound 12 of Example 11.

Claim Rejections – 35 USC § 112

3. The Examiner rejected claims 31-48 for not enabling solvates which were named in the claims. The objected term has been deleted.

Claim Rejections – 35 USC § 103

4. Claims 31, 34-40, and 42-48 are rejected as being unpatentable over Tjoeng (US 5,707,984) and Hsia (US 5,591,710), in view of Anggard (WO99/37616) and MacNee (Eur. J. Pharm. 429, 195-207,2001).

The rejections are respectfully traversed, as the cited documents are not believed to be combinable to provide any compound which would fall into the ambit of the instant application. Moreover, the claims have now been restricted to include the most preferred structures, namely multifunctional steroid compounds; being 1,4 dienes; substituted with keto at position C3; substituted with a nitroxide radical at position C20, and nitrated at positions 11 and 17.

Tjoeng describes a steroid derivatized with nitrite or nitrate esters (Abstract, Summary, Claims). Hsia describes hemoglobin derivatized with nitroxide radicals (Abstract, Summary, Claims), intended for treating oxidative stress (the first paragraph of the Background). Anggard describes piperidine and pyrrolidine derivatized with nitroxide group and nitrate group (pages 6-11, Examples, Claims), for treating oxidative stress (claim 10). MacNee hypothesizes that oxidative stress plays an important role in the injurious and inflammatory responses in airways diseases.

The instant invention, as defined in the amended claims, relates to steroid structures derivatized with nitroxide and nitrate, for use as multifunctional steroids, namely as superior agents in treating a broad range of conditions in which combining those three actions – steroidal, antioxidant, and NO release – is highly efficient. A skilled person would have had to combine the cited documents in a very selective manner. Tjoeng teaches a steroid releasing NO for vascular relaxation (from line 50 at column 1 to line 41 at column 2). The skilled person would have to assume that separating Hsia's nitroxide from proteins and introducing it to Tjoeng's steroids would not abolish their original relaxation properties, and that said nitroxide would further add to them the Hsia's and Anggard's antioxidative features; furthermore, the skilled person would have to assume that MacNee's hypothesis about the relation between oxidative stress and inflammation in the airways diseases might hold also in other systems beside breathing organs, so that the inflammatory action of the derivatized steroid structure would not be diminished by incorporating an antioxidant to the molecule. The applicant respectfully disagrees with the Examiner that the four cited documents would have obviously provided the novel multifunctional structure as claimed in amended claims 31.

5. Claims 32-33 and 41 are rejected as being unpatentable over Tjoeng and Hsia, in view of Anggard and MacNee, and further in view of Burrows (US 5,610,149) and Lerner (US 2,437,261).

Although the applicant believes that the instant PEG conjugates are superior to the cited structures, claims 32-33 and 41 have been canceled at this stage to simplify the prosecution.

Conclusion